

APPLICATION SERIAL NO. 09/719,045

AMENDMENT AND REQ. FOR RECONSIDERATION DATED APRIL 25, 2005

REPLY TO FINAL REJECTION OF MARCH 24, 2004 AND FOLLOWING

NOTICE OF APPEAL FILED ON SEPTEMBER 24, 2004

### STATUS OF THE CLAIMS

The following claim listing replaces all previous listings of the claims.

Please amend the claims as indicated.

Claim 1 (**currently amended**) A divalent antibody fragment comprising two antibody heavy chains and at least one polymer molecule effective for increasing the circulating half-life of said fragment in covalent linkage, each heavy chain being covalently linked to the other by at least one non-disulphide interchain bridge linking the sulphur atom of a cysteine residue in one chain to the sulphur atom of a cysteine residue in the other chain, said cysteine residues being located outside of the variable region domain of each chain, characterised in that the at least one non-disulphide interchain bridge contains a the at least one covalently linked polymer molecule.

Claim 2 (**previously presented**) An antibody fragment according to Claim 1 in which each heavy chain is covalently linked to the other by a single non-disulphide bridge, said bridge containing a covalently linked polymer molecule effective for increasing the circulating half-life of said fragment.

Claim 3 (**previously presented**) An antibody fragment according to Claim 1 wherein each heavy chain is paired with a light chain.

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Claim 4 (**previously presented**) An antibody fragment according to Claim 1 wherein each heavy chain is a  $V_H$ -CH1 chain terminally substituted by a hinge region domain.

Claim 5 (**original**) An antibody fragment according to Claim 4 wherein each non-disulphide bridge present links the sulphur atom of a cysteine residue located in the hinge region domain of one heavy chain, to the sulphur atom of a cysteine residue in the hinge region domain of the other chain.

Claim 6 (**previously presented**) An antibody fragment according to Claim 1 wherein the polymer is an optionally substituted straight or branched chain polymer selected from the group consisting of polyalkylene, polyalkenylene and polyoxyalkylene, or a branched or unbranched polysaccharide.

Claim 7 (**previously presented**) An antibody fragment according to Claim 6 wherein the polymer is an optionally substituted straight or branched chain polymer selected from the group consisting of poly(ethylene glycol) or a derivative of poly(ethylene glycol).

Claim 8 (**withdrawn**) An antibody fragment according to Claim 7 wherein the polymer is selected from the group consisting of methoxy(polyethylene glycol) or a derivative of methoxy(polyethylene glycol).

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Claim 9 (**withdrawn**) An antibody fragment according to Claim 8 wherein the polymer has a molecular weight in the range from about 25000Da to about 40000Da.

Claim 10 (**previously presented**) An antibody fragment according to Claim 1 wherein each interchain bridge is the residue of a homo- or heterobifunctional cross-linking reagent.

Claim 11 (**original**) An antibody fragment according to Claim 10 wherein each bridge is an optionally substituted C<sub>4-20</sub> alkylene chain optionally interrupted by one or more heteroatoms or heteroatom-containing groups.

Claim 12 (**previously presented**) An antibody fragment according to Claim 1 which is covalently attached to one or more effector or reporter molecules.

Claim 13 (**previously presented**) An antibody fragment according to Claim 1 which is able to selectively bind to a cell surface or soluble antigen.

Claim 14 (**original**) An antibody fragment according to Claim 13 wherein the antigen is human tumour necrosis factor- $\alpha$  or a platelet derived growth factor or a receptor thereof.

**DOCKET NO.: CARP0006-100**

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**PATENT**

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Claim 15 **(previously presented)** A pharmaceutical composition comprising an antibody fragment according to any of the preceding claims together with one or more pharmaceutically acceptable excipients, diluents or carriers.